

## **REMARKS**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **I. Status of the Claims and Amendments**

Claims 47 and 48 are requested to be added. Support for new claims 47 and 48 can be found throughout the specification as-filed, including the original claims.

After amending the claims as set forth above, claims 1, 2, 5-24, and 26-46 are pending, and claims 15-17, 21-24, 29, 31-38, and 40-46 are withdrawn. Thus, claims 1, 2, 5-14, 18-20, 26-28, 30, and 39 are pending and subject to examination on the merits.

### **II. Claim Rejections – 35 U.S.C. § 112, First Paragraph**

#### **A. Written Description**

Claims 1, 2, 5-14, 18-20, 26-28, 30 and 39 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description support. According to the Advisory Action, “the amendments to the claims do not change the fact that the claims still recite the production of an enormous number of varied oligosaccharides each of which require distinctly different sets of genes and requires detailed knowledge of the biosynthetic pathways for the synthesis of the desired oligosaccharide, knowledge of the source of all enzymes necessary for such synthesis, knowledge of the metabolic/catabolic pathways present in *E. coli* which would impact on the synthesis/degradation of the desired oligosaccharide and detailed knowledge of how these factors are interrelated such that one obtains the desired result..” Advisory Action at 2. Applicants respectfully traverse this ground of rejection.

In assessing compliance with the written description requirement, “the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed.” MPEP § 2163.02. “The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the

description requirement.” *Id.* Instead, the specification need only describe the claimed invention such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Id.*; MPEP § 2163(I).

Here, the claimed invention is directed to a method for producing an oligosaccharide comprising lactose using a genetically modified cell. The cell comprises “at least one recombinant gene encoding an enzyme capable of modifying said exogenous precursor or one of the intermediates in the biosynthetic pathway of said oligosaccharide.” In addition, the cell “lacks any enzymatic activity liable to degrade said oligosaccharide, said precursor and said intermediates.” This method allows for the production of oligosaccharides in high yield and avoids the use of organic solvents to increase membrane permeability. *See spec. at page 11, ll. 6-10; page 15, ll. 9-11.*

As discussed in detail in Applicants’ response of December 28, 2006, the specification provides a complete description of the presently claim invention. For example, the specification describes the types of precursors that may be used, the genotypes of suitable cells, and synthetic routes to prepare specific oligosaccharides. This teachings is supplemented by actual working examples. Thus, the specification demonstrates that Applicants had possession of the claimed invention.

The Office Action focuses on “the fact that the claims still recite the production of an enormous number of varied oligosaccharides each of which require distinctly different sets of genes and requires detailed knowledge of the biosynthetic pathways.” However, compliance with the written description requirement is based on what is claimed. The claims recite a method involving the use of a genetically modified cell that can internalize precursor to form oligosaccharide. The specification teaches that this method “excludes the standard techniques of membrane permeabilization with organic solvents which block growth and energy metabolism.” Spec. at page 11, ll. 11-12. Thus, high yields of oligosaccharide may be achieved. In addition, this technique also surprisingly avoids lactose killing, as discussed below. Applicants have demonstrated possession of this invention, as discussed in detail in Applicants’ December 28<sup>th</sup> response. Indeed, the specification has a variety of working examples demonstrating possession of the claimed invention.

The rationale set forth by the Office Action ignores the invention as claimed. Rather than assess written description based on the claimed method, which employs a genetically modified cell and internalization of precursor by active transport, the Office Action dramatically expands the scope of written description by requiring a description to support production of every oligosaccharide. Production of every oligosaccharide is not what is claimed, however. Accordingly, the Office Action's rationale in rejecting the claims in lacking written description support is critically flawed.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

**B. Enablement**

Claims 1-14, 18-20, 25-28, 30, and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants respectfully traverse this ground of rejection.

The specification provides sufficient guidance to allow a skilled artisan to practice the presently claimed invention without undue experimentation, as discussed in detail in Applicants December 28<sup>th</sup> response. Indeed, the specification is replete with specific guidance and working examples. This description allows one of skill in the art to make the claimed invention without undue experimentation.

*In re Cook*, 439 F.2d 730 (CCPA 1971) is particularly instructive in the present case. The applicant in *In re Cook* claimed “an optical objective of the zoom type,” i.e., a zoom lens, comprising members having specified numerical relationships. *Id.* at 731. It was “agreed by all that the design of” zoom lenses “is an extremely complex and time-consuming operation” that can take “many months or even years.” *Id.* at 732. The claims were rejected as lacking Section 112 support, because the specification did not enable the production of a zoom lens. The court reversed the rejection by reasoning that although the applicant had “not taught those skilled in the art how to design an entire new zoom lens in short order, it *has* taught those skilled in the art how to design a new zoom lens *of the type here claimed*.” *Id.* at 733 (emphasis original).

Here, the specification provides a method of making oligosaccharide using a genetically modified cell and internalizing exogenous precursor. Accordingly, the claimed invention need not enable production of every oligosaccharide much like Cook was not required to enable the production of a zoom lens.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

**IV. Claim Rejections – 35 U.S.C. § 103**

**A. Bettler in view of Kozumi**

Claims 1, 2, 5-14, 18-20, 26-28, and 39 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Bettler in view of Kozumi. Applicants respectfully traverse this ground of rejection.

As discussed in Applicants' December 28<sup>th</sup> amendment, one of skill in the art would have no motivation to combine Bettler and Kozumi, much less any expectation of success, because it was known in the art that rapid uptake of sugars by lactose permease disrupts membrane function, possibly by causing collapse of the membrane potential. This phenomenon, which results in growth inhibition and eventually cell death, is known as "lactose killing." Given this knowledge in the art, a skilled artisan would have no reason to combine the teachings of Bettler and Kozumi, much less have an expectation of success.

The Advisory Action states that "a skilled artisan would merely have found it obvious to simply allow the cells to grow in the absence of inducer until a desired cell density is achieved and then add the inducer only during the oligosaccharide synthesis step and to keep the amount of inducer low such that lactose killing would be avoided." Advisory Action at 3. However, this explanation is unsupported by the evidence of record. The evidence of record makes clear that lactose killing was a significant problem recognized in the art. *See, e.g.,* Dykhuizen at table 2; Wilson *et al.*, BIOCHIM BIOPHYS ACTA 649(2):377-84 (1981) (Exhibit A); Dykhuizen *et al.*, J. BACTERIOLOGY 135(3):876-82 (1978) (Exhibit B); and Ahmed *et al.*, J GEN MICROBIOL 129(8):2521-29 (1983). In fact, the authors of Dykhuizen conclude on

page 878, column 2, lines 11-17, that “there is strong correlation between the amount of lactose permease and the amount of lactose killing.” Thus, one of skill in the art would not expect that sufficient yields of oligosaccharide could be obtained while avoiding lactose killing. Thus, one of skill in the art would have no reason to perform the claimed method.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

**B. Bettler in view of Kozumi in further view of Johnson and Gotschlich**

Claim 30 stands rejected under 35 U.S.C. § 103 as allegedly obvious over Bettler in view of Kozumi in further view of Johnson and Gotschlich. Applicants respectfully traverse this ground of rejection.

Bettler in view of Kozumi do not teach or suggest the claimed invention, as discussed above, and Johnson and Gotschlich fail to remedy this deficiency. For at least this reason, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

## CONCLUSION

Applicant believes that the present application is now in condition for allowance.  
Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 28, 2006

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